

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-418 (Canceled).

419. (New) A method of reducing the concentration of a metal in an animal in need thereof comprising administering to the animal an effective amount of a peptide having the formula:

$$P_1 - P_2,$$

wherein:

P_1 is:

Xaa₁ Xaa₂ His: or

Xaa₁ Xaa₂ His Xaa₃;

P_2 is (Xaa₄)_n;

Xaa₁ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa₂ is glycine, alanine, β -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa₃ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

Xaa₄ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

420. (New) The method of Claim 419 wherein:

Xaa₁ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, glutamic acid, lysine, hydroxylysine, histidine, arginine, or α -hydroxymethylserine,

Application No.: 10/076,071

Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, glutamine, methionine, lysine, hydroxylysine, histidine, arginine, or α -hydroxymethylserine, and

Xaa₃, when present, is alanine, aspartic acid or lysine.

421. (New) The method of Claim 420 wherein:

Xaa₁ is aspartic acid, glutamic acid, arginine, threonine, or α -hydroxymethylserine,

Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α -hydroxymethylserine, and

Xaa₃, when present, is aspartic acid or lysine.

422. (New) The method of Claim 421 wherein Xaa₁ is aspartic acid or glutamic acid and Xaa₂ is alanine, glycine, valine, threonine, serine, leucine, or α -hydroxymethylserine.

423. (New) The method of Claim 422 wherein Xaa₁ is aspartic acid or glutamic acid and Xaa₂ is alanine, glycine, valine, leucine or isoleucine.

424. (New) The method of Claim 423 wherein P₁ is Asp Ala His, Asp Ala His Asp or Asp Ala His Lys.

425. (New) The method of Claim 424 wherein P₁ is Asp Ala His Lys.

426. (New) The method of Claim 420 wherein Xaa₁ is alanine, serine, threonine, aspartic acid, lysine or histidine and Xaa₂ is glycine, alanine, valine, leucine, isoleucine or histidine.

427. (New) The method of Claim 426 wherein P₁ is Ser Gly His, Thr Leu His or Ala Ala His.
428. The method of Claim 426 wherein P₁ is Lys His His Lys, Asp His His Ala, His Ala His Ala, Ala His His Ala or Asp His His Asp.

429. (New) The method of Claim 419 wherein n is 0-10.

430. (New) The method of Claim 419 wherein P₂ comprises a metal-binding sequence.

431. (New) The method of Claim 430 wherein P₂ comprises one of the following sequences:

(Xaa₄)_m Xaa₃ His Xaa₂ Xaa₅,

(Xaa₄)_m His Xaa₂ Xaa₅,

(Xaa₄)_m Xaa₅ Xaa₂ His Xaa₃, or

(Xaa₄)_m Xaa₅ Xaa₂ His,

wherein Xaa₅ is an amino acid having a free side-chain -NH₂ and m is 0-5.

Application No.: 10/076,071

432. (New) The method of Claim 431 wherein Xaa₅ is Orn or Lys.

433. (New) The method of Claim 430 wherein P₂ comprises one of the following sequences:

[(Xaa₄)_mXaa₅Xaa₂HisXaa₃]_r,

[(Xaa₄)_mXaa₅Xaa₂His]_r,

[(Xaa₄)_mXaa₅Xaa₂HisXaa₃(Xaa₄)_mXaa₅Xaa₂His]_r, or

[(Xaa₄)_mXaa₅Xaa₂His(Xaa₄)_mXaa₅Xaa₂HisXaa₃]_r,

wherein Xaa₅ is an amino acid having a free side-chain -NH₂, m is 0-5 and r is 2-100.

434. (New) The method of Claim 430 wherein P₂ comprises a sequence which binds Cu(I).

435. (New) The method of Claim 434 wherein P₂ comprises one of the following sequences:

Met Xaa₄ Met,

Met Xaa₄ Xaa₄ Met,

Cys Cys,

Cys Xaa₄ Cys,

Cys Xaa₄ Xaa₄ Cys,

Met Xaa₄ Cys Xaa₄ Xaa₄ Cys,

Gly Met Xaa₄ Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:7],

Gly Met Thr Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

γ-Glu Cys Gly.

436. (New) The method of Claim 435 wherein P₂ is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

437. (New) The method of Claim 419 wherein P₂ comprises a sequence which enhances the ability of the peptide to penetrate cell membranes, reach target tissues, or both.

438. (New) The method of Claim 437 wherein P₂ is hydrophobic or an arginine oligomer.

439. (New) The method of Claim 419 wherein at least one of the amino acids of P₁ other than β-alanine, when present, is a D-amino acid.

440. (New) The method of Claim 439 wherein Xaa₁ is a D-amino acid, His is a D-amino acid, or both Xaa₁ and His are D-amino acids.

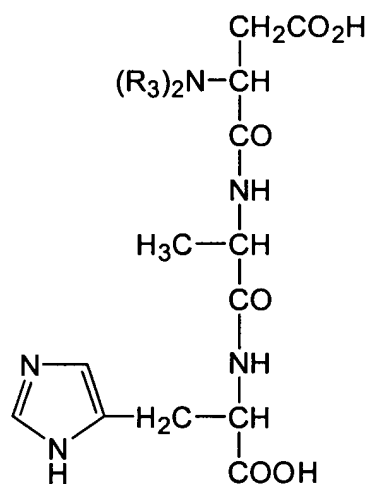
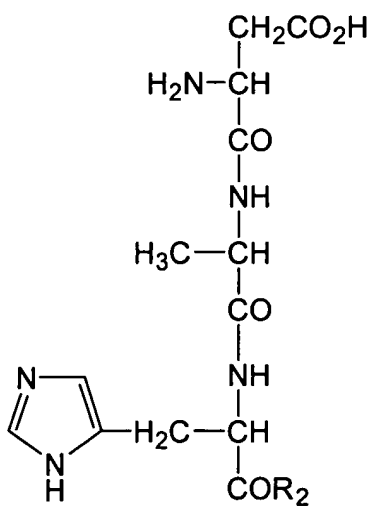
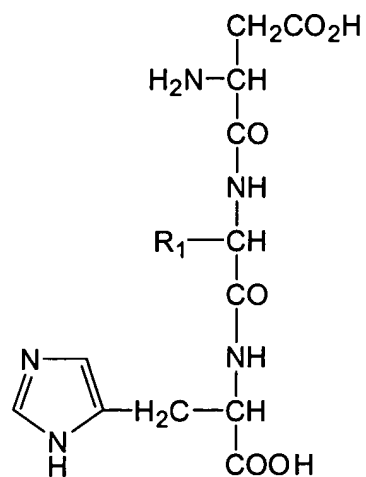
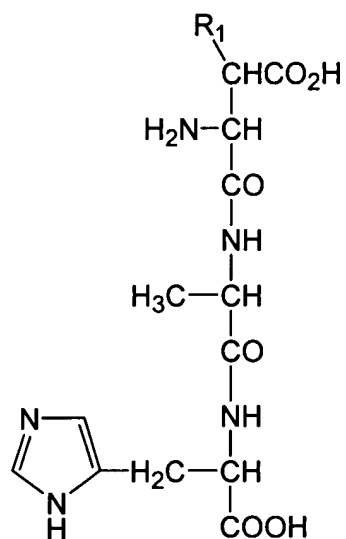
441. (New) The method of Claim 440 wherein all of the amino acids of P₁ other than β -alanine, when present, are D-amino acids.

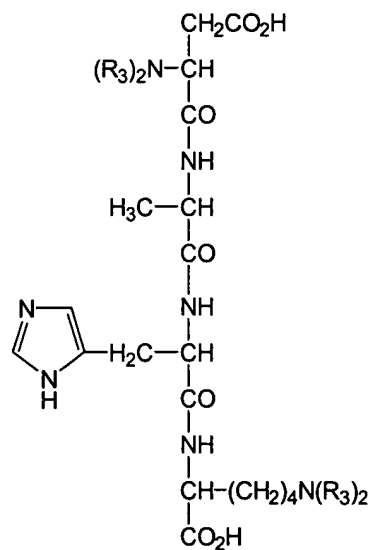
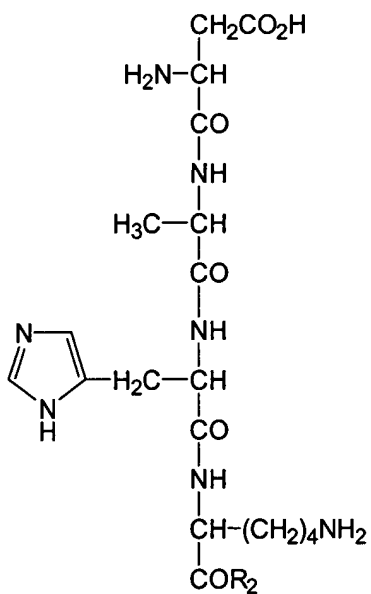
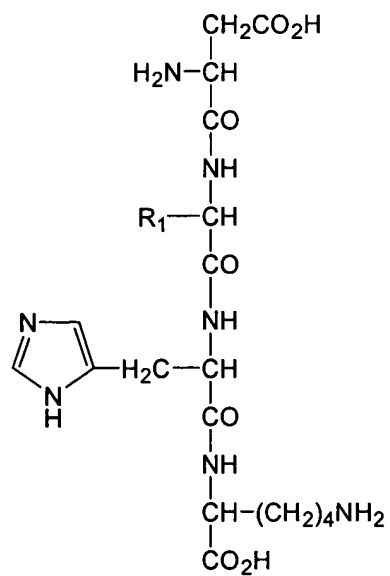
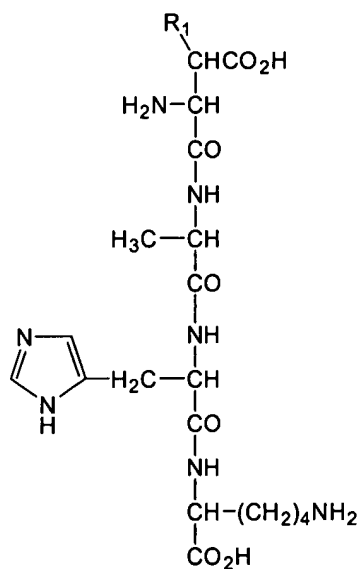
442. (New) The method of Claim 439 wherein at least 50% of the amino acids of P₂ are D-amino acids.

443. (New) The method of Claim 419 wherein at least one amino acid of P₁, at least one amino acid of P₂, or at least one amino acid of P₁ and at least one amino acid of P₂ is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of P₁ to bind metal ions, (b) a substituent that protects the peptide from proteolytic enzymes without altering the ability of P₁ to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that improves the ability of the peptide to bind metal ions.

444. (New) The method of Claim 443 wherein the terminal -COOH of P₁ or P₂ is substituted to produce -COR₂, wherein R₂ is -NH₂, -NHR₁, -N(R₁)₂, -OR₁, or -R₁, wherein R₁ is an alkyl, aryl or heteroaryl.

445. (New) The method of Claim 443 wherein n is 0 and P₁ has one of the following formulas:





wherein:

R_1 is an alkyl, aryl, or heteroaryl;

R_2 is $-NH_2$, $-NHR_1$, $N(R_1)_2$, $-OR_1$, or R_1 ; and

Application No.: 10/076,071

R₃ is H, a non-peptide, metal-binding functional group or the two R₃ groups together form a non-peptide, metal-binding functional group.

446. (New) The method of Claim 445 wherein R₂ is -NH₂.

447. (New) The method of Claim 419 wherein the method further comprises administering an effective amount of another metal-binding compound in combination with the peptide.

448. (New) The method of Claim 447 wherein the metal-binding compound binds iron.

449. (New) The method of Claim 448 wherein the iron-binding compound is deferoxamine mesylate.

450. (New) The method of Claim 447 wherein the metal-binding compound binds Cu(I).

451. (New) The method of Claim 450 wherein the Cu(I)-binding compound is a peptide.

452. (New) The method of Claim 451 wherein the Cu(I)-binding peptide comprises one of the following sequences:

Met Xaa₄ Met,

Met Xaa₄ Xaa₄ Met,

Cys Cys

Cys Xaa₄ Cys,

Cys Xaa₄ Xaa₄ Cys,

Met Xaa₄ Cys Xaa₄ Xaa₄ Cys,

Gly Met Xaa₄ Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:7],

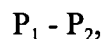
Gly Met Thr Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

γ-Glu Cys Gly,

wherein Xaa₄ is any amino acid.

453. (New) A method of treating an angiogenic disease or condition in an animal comprising administering to the animal an effective amount of a peptide having the formula:



wherein:

P₁ is:

Application No.: 10/076,071

Xaa₁ Xaa₂ His: or

Xaa₁ Xaa₂ His Xaa₃;

P₂ is (Xaa₄)_n;

Xaa₁ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa₂ is glycine, alanine, β -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa₃ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

Xaa₄ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

454. (New) The method of Claim 453 wherein:

Xaa₁ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, glutamic acid, lysine, hydroxylysine, histidine, arginine, or α -hydroxymethylserine,

Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, glutamine, methionine, lysine, hydroxylysine, histidine, arginine, or α -hydroxymethylserine, and

Xaa₃, when present, is alanine, aspartic acid or lysine.

455. (New) The method of Claim 454 wherein:

Xaa₁ is aspartic acid, glutamic acid, arginine, threonine, or α -hydroxymethylserine,

Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α -hydroxymethylserine, and

Xaa₃, when present, is aspartic acid or lysine.

456. (New) The method of Claim 455 wherein Xaa₁ is aspartic acid or glutamic acid and Xaa₂ is alanine, glycine, valine, threonine, serine, leucine, or α -hydroxymethylserine.

457. (New) The method of Claim 456 wherein Xaa₁ is aspartic acid or glutamic acid and Xaa₂ is alanine, glycine, valine, leucine or isoleucine.

458. (New) The method of Claim 457 wherein P₁ is Asp Ala His, Asp Ala His Asp or Asp Ala His Lys.

459. (New) The method of Claim 458 wherein P₁ is Asp Ala His Lys.

460. (New) The method of Claim 454 wherein Xaa₁ is alanine, serine, threonine, aspartic acid, lysine or histidine and Xaa₂ is glycine, alanine, valine, leucine, isoleucine or histidine.

461. (New) The method of Claim 460 wherein P₁ is Ser Gly His, Thr Leu His or Ala Ala His.

462. (New) The method of Claim 460 wherein P₁ is Lys His His Lys, Asp His His Ala, His Ala His Ala, Ala His His Ala or Asp His His Asp.

463. (New) The method of Claim 453 wherein n is 0-10.

464. (New) The method of Claim 453 wherein P₂ comprises a metal-binding sequence.

465. (New) The method of Claim 464 wherein P₂ comprises one of the following sequences:

(Xaa₄)_m Xaa₃ His Xaa₂ Xaa₅,
(Xaa₄)_m His Xaa₂ Xaa₅,
(Xaa₄)_m Xaa₅ Xaa₂ His Xaa₃, or
(Xaa₄)_m Xaa₅ Xaa₂ His,

wherein Xaa₅ is an amino acid having a free side-chain -NH₂ and m is 0-5.

466. (New) The method of Claim 465 wherein Xaa₅ is Orn or Lys.

467. (New) The method of Claim 464 wherein P₂ comprises one of the following sequences:

[(Xaa₄)_m Xaa₅ Xaa₂ His Xaa₃]_r,
[(Xaa₄)_m Xaa₅ Xaa₂ His]_r,
[(Xaa₄)_m Xaa₅ Xaa₂ His Xaa₃ (Xaa₄)_m Xaa₅ Xaa₂ His]_r, or
[(Xaa₄)_m Xaa₅ Xaa₂ His (Xaa₄)_m Xaa₅ Xaa₂ His Xaa₃]_r,

wherein Xaa₅ is an amino acid having a free side-chain -NH₂, m is 0-5 and r is 2-100.

468. (New) The method of Claim 464 wherein P₂ comprises a sequence which binds Cu(I).

469. (New) The method of Claim 468 wherein P₂ comprises one of the following sequences:

Met Xaa₄ Met,

Met Xaa₄ Xaa₄ Met,

Cys Cys,

Cys Xaa₄ Cys,

Cys Xaa₄ Xaa₄ Cys,

Met Xaa₄ Cys Xaa₄ Xaa₄ Cys,

Gly Met Xaa₄ Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:7],

Gly Met Thr Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

γ-Glu Cys Gly.

470. (New) The method of Claim 469 wherein P₂ is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

471. (New) The method of Claim 453 wherein P₂ comprises a sequence which enhances the ability of the peptide to penetrate cell membranes, reach target tissues, or both.

472. (New) The method of Claim 471 wherein P₂ is hydrophobic or an arginine oligomer.

473. (New) The method of Claim 453 wherein at least one of the amino acids of P₁ other than β-alanine, when present, is a D-amino acid.

474. (New) The method of Claim 473 wherein Xaa₁ is a D-amino acid, His is a D-amino acid, or both Xaa₁ and His are D-amino acids.

475. (New) The method of Claim 474 wherein all of the amino acids of P₁ other than β-alanine, when present, are D-amino acids.

476. (New) The method of Claim 475 wherein at least 50% of the amino acids of P₂ are D-amino acids.

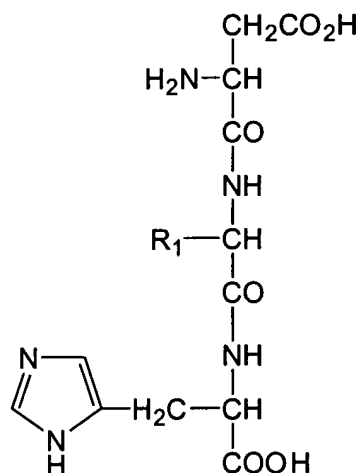
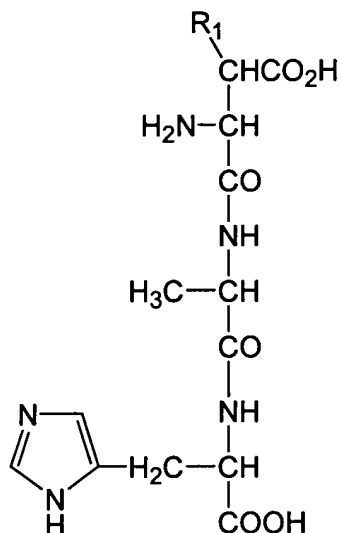
477. (New) The method of Claim 453 wherein at least one amino acid of P₁, at least one amino acid of P₂, or at least one amino acid of P₁ and at least one amino acid of P₂ is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of P₁ to bind metal ions, (b) a substituent that protects the peptide from proteolytic enzymes without altering

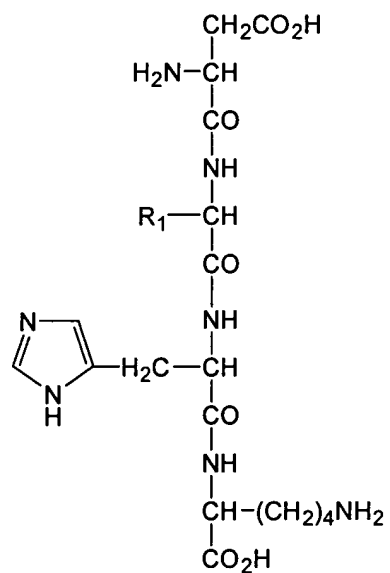
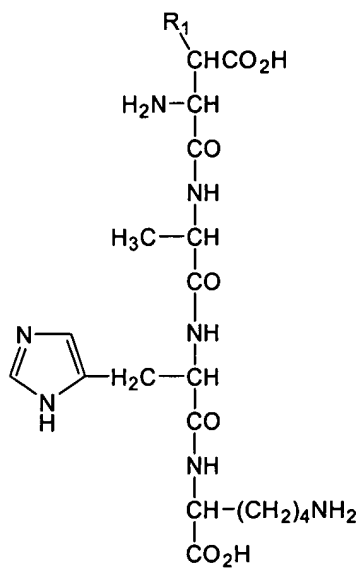
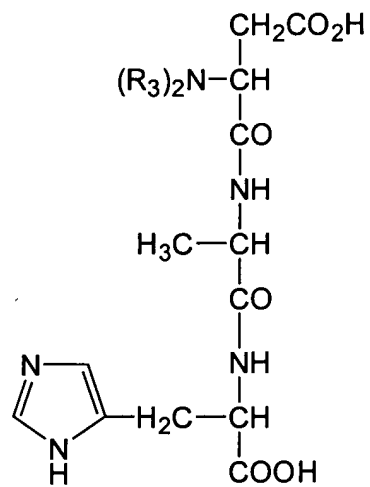
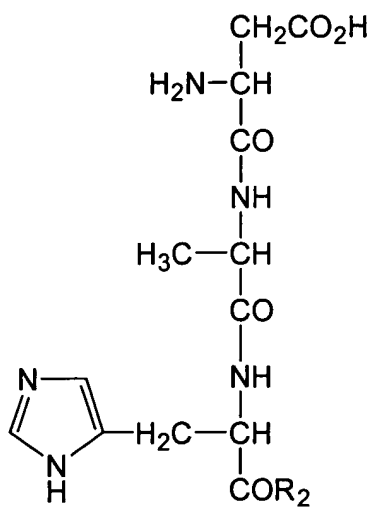
Application No.: 10/076,071

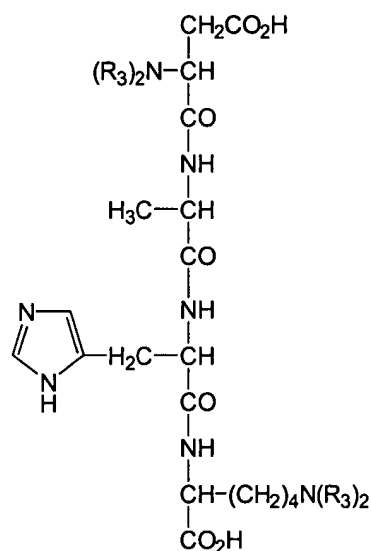
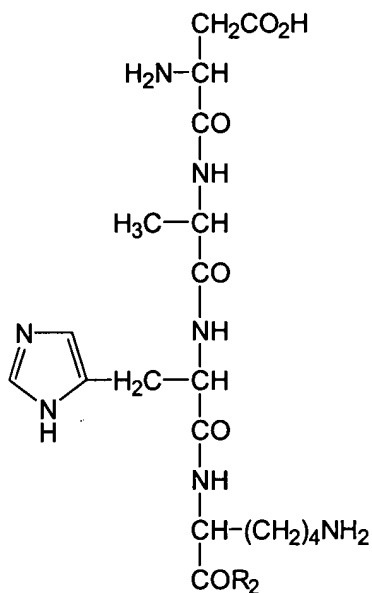
the ability of P_1 to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that improves the ability of the peptide to bind metal ions.

478. (New) The method of Claim 477 wherein the terminal $-\text{COOH}$ of P_1 or P_2 is substituted to produce $-\text{COR}_2$, wherein R_2 is $-\text{NH}_2$, $-\text{NHR}_1$, $-\text{N}(\text{R}_1)_2$, $-\text{OR}_1$, or $-\text{R}_1$, wherein R_1 is an alkyl, aryl or heteroaryl.

479. (New) The method of Claim 477 wherein n is 0 and P_1 has one of the following formulas:







wherein:

R_1 is an alkyl, aryl, or heteroaryl;

R_2 is $-NH_2$, $-NHR_1$, $N(R_1)_2$, $-OR_1$, or R_1 ; and

R_3 is H, a non-peptide, metal-binding functional group or the two R_3 groups together form a non-peptide, metal-binding functional group.

480. (New) The method of Claim 479 wherein R_2 is $-NH_2$.

481. The method of Claim 453 wherein the method further comprises administering an effective amount of another metal-binding compound in combination with the peptide.

482. (New) The method of Claim 481 wherein the metal-binding compound binds iron.

484. (New) The method of Claim 482 wherein the iron-binding compound is deferoxamine mesylate.

485. (New) The method of Claim 481 wherein the metal-binding compound binds Cu(I).

486. (New) The method of Claim 485 wherein the Cu(I)-binding compound is a peptide.

487. (New) The method of Claim 486 wherein the Cu(I)-binding peptide comprises one of the following sequences:

Met Xaa₄ Met,
Met Xaa₄ Xaa₄ Met,
Cys Cys
Cys Xaa₄ Cys,
Cys Xaa₄ Xaa₄ Cys,
Met Xaa₄ Cys Xaa₄ Xaa₄ Cys,
Gly Met Xaa₄ Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:7],
Gly Met Thr Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:8],
Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or
γ-Glu Cys Gly,

wherein Xaa₄ is any amino acid.

488. (New) The method of Claim 453 wherein the angiogenic disease or condition is a neoplastic disease, a connective tissue disorder, psoriasis, an ocular angiogenic disease, a cardiovascular disease, a cerebral vascular disease, hemophiliac joints, an immune disorder, a benign tumor, hypertrophy, endometriosis, polyposis, or obesity.

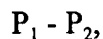
489. (New) The method of Claim 488 wherein the angiogenic disease or condition is a neoplastic disease is a tumor.

490. (New) The method of Claim 489 wherein the neoplastic disease is a tumor.

491. (New) The method of Claim 490 wherein the tumor is located in the bladder, brain, breast, cervix, colon, rectum, kidney, lung, ovary, pancreas, prostate, stomach or uterus.

492. (New) The method of Claim 489 wherein the neoplastic disease is tumor metastasis.

493. (New) A method of treating cancer or inhibiting carcinogenesis in an animal comprising administering to the animal an effective amount of a peptide having the formula:



wherein:

P₁ is:

Application No.: 10/076,071

Xaa₁ Xaa₂ His: or

Xaa₁ Xaa₂ His Xaa₃;

P₂ is (Xaa₄)_n;

Xaa₁ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa₂ is glycine, alanine, β -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or α -hydroxymethylserine;

Xaa₃ is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

Xaa₄ is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

494. (New) The method of Claim 493 wherein:

Xaa₁ is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, glutamic acid, lysine, hydroxylysine, histidine, arginine, or α -hydroxymethylserine,

Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, glutamine, methionine, lysine, hydroxylysine, histidine, arginine, or α -hydroxymethylserine, and

Xaa₃, when present, is alanine, aspartic acid or lysine.

495. (New) The method of Claim 494 wherein:

Xaa₁ is aspartic acid, glutamic acid, arginine, threonine, or α -hydroxymethylserine,

Xaa₂ is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or α -hydroxymethylserine, and

Xaa₃, when present, is aspartic acid or lysine.

496. (New) The method of Claim 495 wherein Xaa₁ is aspartic acid or glutamic acid and Xaa₂ is alanine, glycine, valine, threonine, serine, leucine, or α -hydroxymethylserine.

497. (New) The method of Claim 496 wherein Xaa₁ is aspartic acid or glutamic acid and Xaa₂ is alanine, glycine, valine, leucine or isoleucine.

498. (New) The method of Claim 497 wherein P₁ is Asp Ala His, Asp Ala His Asp or Asp Ala His Lys.

499. (New) The method of Claim 498 wherein P₁ is Asp Ala His Lys.

500. (New) The method of Claim 494 wherein Xaa₁ is alanine, serine, threonine, aspartic acid, lysine or histidine and Xaa₂ is glycine, alanine, valine, leucine, isoleucine or histidine.

501. (New) The method of Claim 500 wherein P₁ is Ser Gly His, Thr Leu His or Ala Ala His.

502. (New) The method of Claim 500 wherein P₁ is Lys His His Lys, Asp His His Ala, His Ala His Ala, Ala His His Ala or Asp His His Asp.

503. (New) The method of Claim 493 wherein n is 0-10.

504. (New) The method of Claim 493 wherein P₂ comprises a metal-binding sequence.

505. (New) The method of Claim 504 wherein P₂ comprises one of the following sequences:

(Xaa₄)_m Xaa₃ His Xaa₂ Xaa₅,
(Xaa₄)_m His Xaa₂ Xaa₅,
(Xaa₄)_m Xaa₅ Xaa₂ His Xaa₃, or
(Xaa₄)_m Xaa₅ Xaa₂ His,

wherein Xaa₅ is an amino acid having a free side-chain -NH₂ and m is 0-5.

506. (New) The method of Claim 505 wherein Xaa₅ is Orn or Lys.

507. (New) The method of Claim 504 wherein P₂ comprises one of the following sequences:

[(Xaa₄)_mXaa₅Xaa₂HisXaa₃]_r,
[(Xaa₄)_mXaa₅Xaa₂His]_r,
[(Xaa₄)_mXaa₅Xaa₂HisXaa₃(Xaa₄)_mXaa₅Xaa₂His]_r, or
[(Xaa₄)_mXaa₅Xaa₂His(Xaa₄)_mXaa₅Xaa₂HisXaa₃]_r,

wherein Xaa₅ is an amino acid having a free side-chain -NH₂, m is 0-5 and r is 2-100.

508. (New) The method of Claim 504 wherein P₂ comprises a sequence which binds Cu(I).

509. (New) The method of Claim 508 wherein P_2 comprises one of the following sequences:

Met Xaa₄ Met,

Met Xaa₄ Xaa₄ Met,

Cys Cys,

Cys Xaa₄ Cys,

Cys Xaa₄ Xaa₄ Cys,

Met Xaa₄ Cys Xaa₄ Xaa₄ Cys,

Gly Met Xaa₄ Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:7],

Gly Met Thr Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

γ -Glu Cys Gly.

510. (New) The method of Claim 509 wherein P_2 is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

511. (New) The method of Claim 493 wherein P_2 comprises a sequence which enhances the ability of the peptide to penetrate cell membranes, reach target tissues, or both.

512. (New) The method of Claim 511 wherein P_2 is hydrophobic or an arginine oligomer.

513. (New) The method of Claim 493 wherein at least one of the amino acids of P_1 other than β -alanine, when present, is a D-amino acid.

514. (New) The method of Claim 513 wherein Xaa₁ is a D-amino acid, His is a D-amino acid, or both Xaa₁ and His are D-amino acids.

515. (New) The method of Claim 514 wherein all of the amino acids of P_1 other than β -alanine, when present, are D-amino acids.

516. (New) The method of Claim 513 wherein at least 50% of the amino acids of P_2 are D-amino acids.

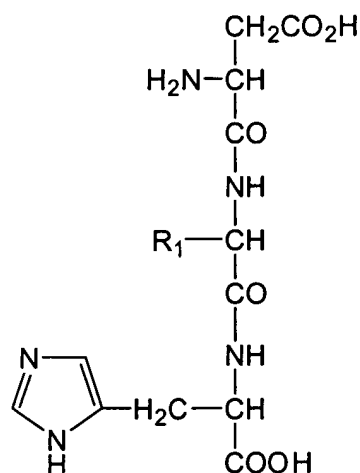
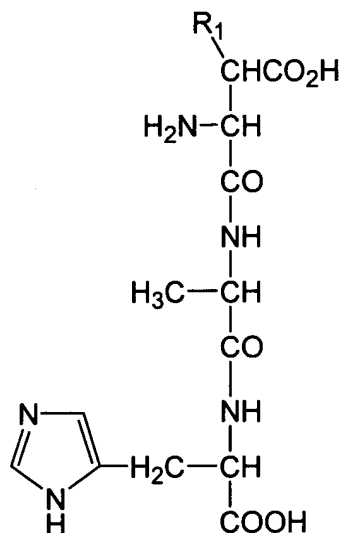
517. (New) The method of Claim 493 wherein at least one amino acid of P_1 , at least one amino acid of P_2 , or at least one amino acid of P_1 and at least one amino acid of P_2 is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of P_1 to bind metal ions, (b) a substituent that protects the peptide from proteolytic enzymes without altering

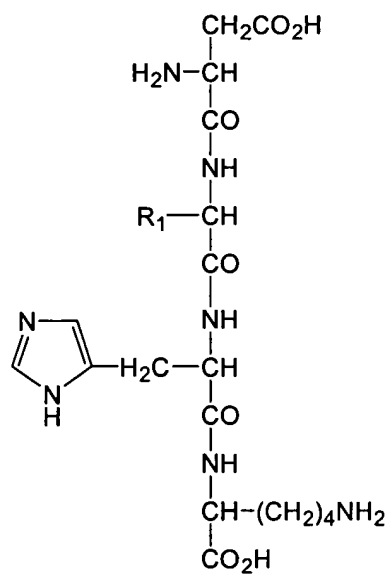
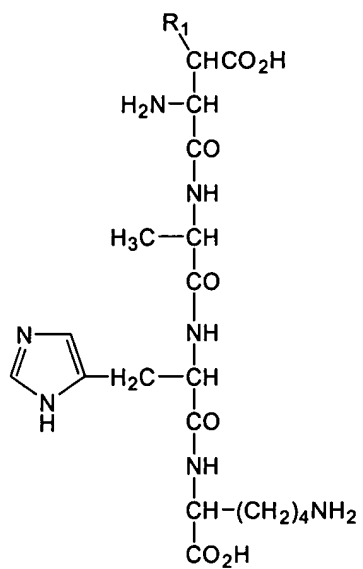
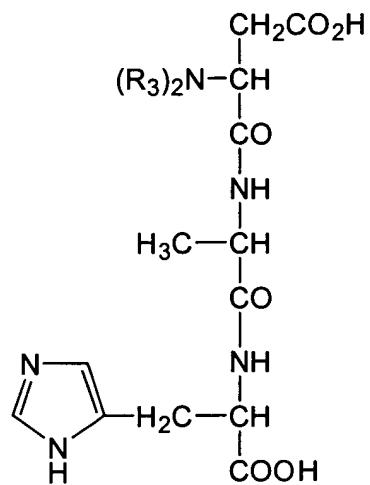
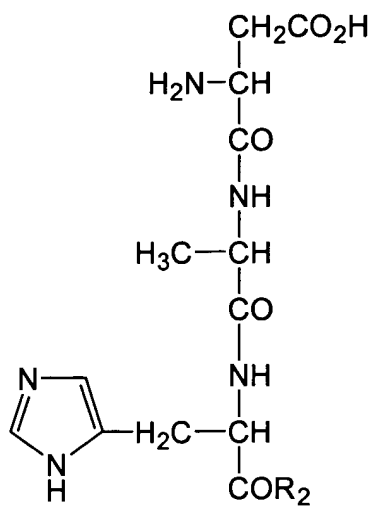
Application No.: 10/076,071

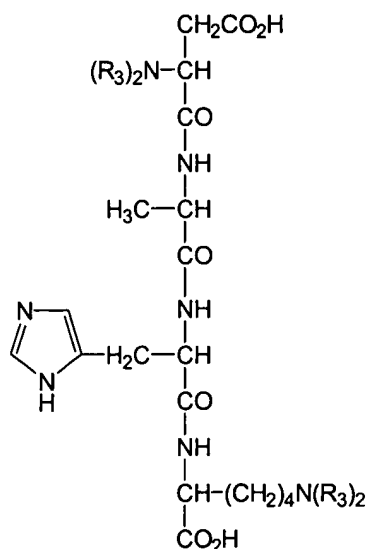
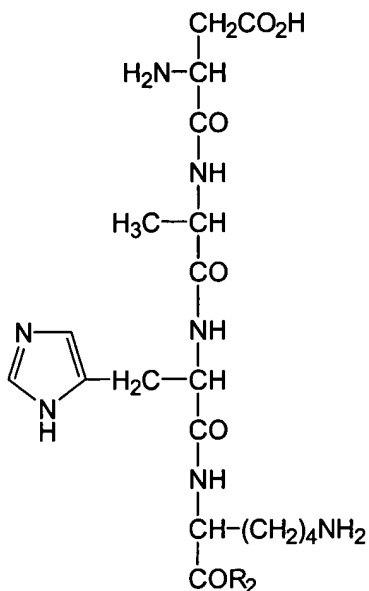
the ability of P_1 to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that improves the ability of the peptide to bind metal ions.

518. (New) The method of Claim 517 wherein the terminal $-\text{COOH}$ of P_1 or P_2 is substituted to produce $-\text{COR}_2$, wherein R_2 is $-\text{NH}_2$, $-\text{NHR}_1$, $-\text{N}(\text{R}_1)_2$, $-\text{OR}_1$, or $-\text{R}_1$, wherein R_1 is an alkyl, aryl or heteroaryl.

519. (New) The method of Claim 517 wherein n is 0 and P_1 has one of the following formulas:







R₁ is an alkyl, aryl, or heteroaryl;

R_2 is $-NH_2$, $-NHR_1$, $N(R_1)_2$, $-OR_1$, or R_1 ; and

R₃ is H, a non-peptide, metal-binding functional group or the two R₃ groups together form a non-peptide, metal-binding functional group.

520. (New) The method of Claim 519 wherein R₇ is -NH₂.

521. (New) The method of Claim 493 wherein the method further comprises administering an effective amount of another metal-binding compound in combination with the peptide.

522. (New) The method of Claim 521 wherein the metal-binding compound binds iron.

523. (New) The method of Claim 522 wherein the iron-binding compound is deferoxamine mesylate.

524. (New) The method of Claim 521 wherein the metal-binding compound binds Cu(I).

525. (New) The method of Claim 524 wherein the Cu(I)-binding compound is a peptide.

Application No.: 10/076,071

526. (New) The method of Claim 525 wherein the Cu(I)-binding peptide comprises one of the following sequences:

Met Xaa₄ Met,

Met Xaa₄ Xaa₄ Met,

Cys Cys

Cys Xaa₄ Cys,

Cys Xaa₄ Xaa₄ Cys,

Met Xaa₄ Cys Xaa₄ Xaa₄ Cys,

Gly Met Xaa₄ Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:7],

Gly Met Thr Cys Xaa₄ Xaa₄ Cys [SEQ ID NO:8],

Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or

γ-Glu Cys Gly,

wherein Xaa₄ is any amino acid.

527. (New) The method of Claim 493 wherein the cancer is located in the kidney, liver, colon, breast, gastrointestinal tract or brain.

528. (New) The method of Claim 493 wherein the cancer is metastatic cancer.

529. (New) The method of Claim 493 wherein the cancer comprises a tumor.

530. (New) The method of Claim 529 wherein the tumor is located in the bladder, brain, breast, cervix, colon, rectum, kidney, lung, ovary, pancreas, prostate, stomach or uterus.